News Release

December 22, 2020
JCR Pharmaceuticals Co., Ltd.

Translation

JCR Files for Marketing Approval of JR-141 (alfapabinafuspe) for Hunter Syndrome in Brazil

December 22, 2020 -- JCR Pharmaceuticals Co., Ltd. (TSE 4552; Chairman and President: Shin Ashida; "JCR") announced today that it has filed an application with the Brazilian Health Surveillance Agency (Agência Nacional de Vigilância Sanitária) [ANVISA] for marketing approval of JR-141 (Brazilian Common Denomination: alfapabinafuspe) for the treatment of mucopolysaccharidosis II (Hunter syndrome).
JR-141 is a blood-brain-barrier (BBB)-penetrating recombinant iduronate-2-sulfatase product candidate for the treatment of patients with Hunter syndrome, to which J-Brain Cargo®, JCR's proprietary BBB technology, is applied.

This filing for marketing approval is based on evidence comprehensively supported by the results obtained to date from non-clinical and clinical trials with JR-141 in Japan and Brazil.
In a phase 2 clinical trial conducted in Brazil, JR-141 was administered to patients for 26 weeks. With regard to the efficacy endpoints, a decrease in heparan sulfate (HS) concentrations in cerebrospinal fluid (CSF), the biomarker for effectiveness against central nervous system (CNS) symptoms, was observed in all patients that received 2mg/kg/week or more. The trial also confirmed a decrease of dermatan sulfate (DS) concentration in blood in enzyme-replacement-therapy (ERT)-naïve subjects, and stabilization in patients switched from standard ERT to JR-141. Assessment of neurocognitive development demonstrated maintenance or improvement of age-equivalent function in most subjects during the 26 weeks of treatment. 52 weeks follow-up data confirmed a neurocognitive benefit in both severe and attenuated patients.
The profile of adverse events concluded that JR-141 can be safely administered as long-term treatment to patients with MPS II. No drug-related serious adverse events were reported.

Following JR-141, JCR plans to harness its J-Brain Cargo® technology platform and develop a robust pipeline of innovative ERT products for additional lysosomal storage disorders (LSDs). JCR, as a specialty pharma in the rare disease arena, will continue to proactively engage in research and development of transformative treatment options for patients with rare diseases.

This filing for marketing approval is expected to have a minor impact on JCR's consolidated financial results for the year ending on March 31, 2021.

About JR-141
JR-141 is a recombinant fusion protein of an antibody against the human transferrin receptor and idursulfase, the enzyme that is missing or malfunctioning in subjects with Hunter syndrome. It is

expected to be effective against CNS symptoms by crossing the BBB through transferrin receptor-mediated transcytosis using J-Brain Cargo®, JCR's proprietary BBB technology. Uptake into cells is mediated through the mannose-6-phosphate receptor. JCR has advanced development activities by establishing the necessary evidence from the molecular design stage to the non-clinical and clinical trial phases.
In non-clinical trials, JCR has confirmed both high affinity binding of JR-141 to transferrin receptors, and passage across the BBB into neuronal cells as evidenced by electron microscopy. In addition, JCR has confirmed that using J-Brain Cargo® technology, enzymes are taken up into various brain tissues. A decrease in substrate accumulation has also been confirmed in an animal model of Hunter syndrome.*[1]
In several clinical trials of JR-141, JCR obtained evidence of reduction of heparan sulfate concentrations in the CSF, a biomarker for assessing effectiveness against CNS symptoms, consistent with the results obtained from non-clinical studies. JCR also obtained clinical results that demonstrate positive effects of JR-141 on CNS symptoms.*[2]

About mucopolysaccharidosis II (Hunter syndrome)
Mucopolysaccharidosis II (Hunter syndrome) is an X-linked recessive LSD caused by a deficiency of iduronate-2-sulfatase, an enzyme that breaks down glycosaminoglycans (mucopolysaccharides) in the body. The number of patients with Hunter syndrome in worldwide is estimated at approximately 7,800 (according to JCR research). Data from the MPS Brazil Network indicate that MPS II is the most common type of MPS in the country, with 343 cases diagnosed between 1982 and 2015*[3]. Hunter syndrome gives rise to a wide range of somatic and neurological symptoms. A major limitation to current ERT is that it does not address CNS symptoms because of the enzyme's inability cross the BBB.

<References>
*[1]: Hiroyuki Sonoda, et al. A Blood-Brain-Barrier-Penetrating Anti-human Transferrin Receptor Antibody Fusion Protein for Neuronopathic Mucopolysaccharidosis II. Mol Ther. 2018; 26(5): 1366-74.
*[2]: Torayuki Okuyama, et al. Iduronate-2-sulfatase with Anti-human Transferrin Receptor Antibody for Neuropathic Mucopolysaccharidosis II: A Phase 1/2 Trial. Mol Ther. 2020; 27(2): 456-464.
*[3]: Giugliani R, et al. Relative frequency and estimated minimal frequency of Lysosomal Storage Diseases in Brazil: Report from a Reference Laboratory. Genet Mol Biol. 2017; 40: 31–39.

[About JCR Pharmaceuticals]
JCR is a specialty pharmaceutical company engaged in the research, development, manufacturing and marketing of biopharmaceuticals and regenerative medicine with a focus on rare diseases. Its philosophy, "Contributing towards people's healthcare through pharmaceutical products" drives JCR to create innovative pharmaceutical products as value-added treatment options for the under-served patient populations.

[Cautionary Statement Regarding Forward-Looking Statements]
This document contains forward-looking statements that are subject to known and unknown risks and uncertainties, many of which are outside our control. Forward-looking statements often contain words such as "believe," "estimate," "anticipate," "intend," "plan," "will," "would," "target" and similar references to future periods. All forward-looking statements regarding our plans, outlook, strategy and future business, financial performance and financial condition are based on judgments derived from the information available to us at this time. Factors or events that could cause our actual results to be materially different from those expressed in our forward-looking statements include, but are not limited to, a deterioration of economic conditions, a change in the legal or governmental system, a delay in launching a new product, impact on competitors'

pricing and product strategies, a decline in marketing capabilities relating to our products, manufacturing difficulties or delays, an infringement of our intellectual property rights , an adverse court decision in a significant lawsuit and regulatory actions.
This document involves information on pharmaceutical products (including those under development). However, it is not intended for advertising or providing medical advice. Furthermore, it is intended to provide information on our company and businesses and not to solicit investment in securities we issue.
Except as required by law, we assume no obligation to update these forward-looking statements publicly or to update the factors that could cause actual results to differ materially, even if new information becomes available in the future.

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